INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2005/004123

A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl[7] A61K38/16, A23L1/305, A61K38/00, A61P35/00, 37/04, 43/00//C07K14/47

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int.Cl[7] A61K38/16, A23L1/305, A61K38/00, A61P35/00, 37/04, 43/00//C07K14/47

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Jitsuyo Shinan Koho 1922-1996 Jitsuyo Shinan Toroku Koho 1996-2005
Kokai Jitsuyo Shinan Koho 1971-2005 Toroku Jitsuyo Shinan Koho 1994-2005

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAP(STN), REGISTRY(STN), BIOSIS(STN), MEDLINE(STN), EMBASE(STN), WPIDS(STN), JOIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	Takuma SAKURAI et al., 'Lactoferrin Bunkaibutsu (LFH) no Rituximab ni yoru Hotai Izonsei no Saibu Shogai Sayo (CDC) ni Oyobosu Tenka Koka', The Japanese Cancer Association Sokai Kiji, (25 August, 2004 (25.08.04)), Vol.63RD, page 308, P-0799	1-24
P,X	Takuma SAKURAI et al., 'Rituximab ni yoru Hotai Izonsei no Saibo Shogai Sayo (CDC) ni Oyobosu Lactoferrin Bunkaibutsu (LFH) no Tenka Koka', Rinsho Ketsueki, (30 August, 2004 (30.08.04)), Vol.45, No.8, page 915, PS-2-186	1-24

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 June, 2005 (22.06.05)	05 July, 2005 (05.07.05)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (January 2004)

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International application No.
PCT/JP2005/004123

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP 2002-515893 A (Famingu Interekuchuaru Puropati Bibui), 28 May, 2002 (28.05.02), Full text; Claims; page 24, 3rd line from the bottom; page 52, 5th line from the bottom & WO 98/33509 A2 & AU 9863076 B & EP 1017407 A2 & US 6333311 B	1-24
A	IIGO, M. et al., 'INHIBITORY EFFECTS OF BOVINE LACTOFERRIN ON COLON CARCINOMA 26 LUNG METASTASIS IN MICE.', CLIN.EXP.METASTASIS, (1999), Vol.17, No.1, pages 35 to 40, full text, REGISTRY NO.146897-68-9	1-24
A	WO 00/12542 A2 (ALPHARMA AS), 09 March, 2000 (09.03.00), Full text; Claim 21; example 16; REGISTRY NO.170867-20-6 & AU 9955268 B & EP 1109827 A2 & US 2003/22821 A1 & US 2003/148936 A1	1-24
A	ELIASSEN, LT. et al., 'EVIDENCE FOR A DIRECT ANTITUMOR MECHANISM OF ACTION OF BOVINE LACTOFERRICIN.', ANTICANCER RES., (2002), Vol.22, No.5, pages 2703 to 2710, full text, REGISTRY NO.146897-68-9	1-24
A	JP 2002-523517 A (ALPHARMA AS), 30 July, 2002 (30.07.02), Full text; Claims; example 5; REGISTRY NO.170867-20-6 & WO 00/12541 A2 & AU 9955267 B & EP 1109831 A2	1-24
A	JP 10-59864 A (Morinaga Milk Industry Co., Ltd.), 03 March, 1998 (03.03.98), Full text; REGISTRY NO.146897-68-9 & WO 98/6424 A1 REGISTRY NO.146897-68-9	1-24
A	YOO, YC. et al., 'BOVINE LACTOFERRIN AND LACTOFERRICIN INHIBIT TUMOR METASTASIS IN MICE.', ADV.EXP.MED.BIOL., (1998), Vol.443, pages 285 to 291, full text, REGISTRY NO.146897-68-9	1-24
A	YOO, YC. et al., 'APOPTOSIS IN HUMAN LEUKEMIC CELLS INDUCED BY LACTOFERRICIN, A BOVINE MILK PROTEIN-DERIVED PEPTIDE: INVOLVEMENT OF REACTIVE OXYGEN SPECIES.', BIOCHEM.BIOPHYS. RES.COMMUN., (1997), Vol.237, No.3, pages 624 to 628, full text, REGISTRY NO.146897-68-9	1-24

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2005/004123

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	YOO, YC. et al., 'BOVINE LACTOFERRIN AND LACTOFERRICIN, A PEPTIDE DERIVED FROM BOVINE LACTOFERRIN, INHIBIT TUMOR METASTASIS IN MICE.', JPN.J.CANCER RES., (1997), Vol.88, No.2, pages 184 to 190, full text, REGISTRY NO.146897-68-9	1-24
A	ELIASSEN, LT. et al., 'ENHANCED ANTITUMOUR ACTIVITY OF 15-RESIDUE BOVINE LACTOFERRICIN DERIVATIVES CONTAINING BULKY AROMATIC AMINO ACIDS AND LIPOPHILIC N-TERMINAL MODIFICATION.', JOURNAL OF PEPTIDE SCIENCE, (2003), Vol.9, pages 510 to 517, full text, REGISTRY NO.146897-68-9	1-24
A	JP 8-73499 A (Snow Brand Milk Products Co., Ltd.), 19 March, 1996 (19.03.96), Full text; REGISTRY NO.170867-20-6 (Family: none)	1-24
A	JP 7-309771 A (Morinaga Milk Industry Co., Ltd.), 28 November, 1995 (28.11.95), Full text; REGISTRY NO.170867-20-6 (Family: none)	1-24

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Box No. II **Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [x] Claims Nos.: 25, 26
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 25 and 26 involve embodiments concerning methods for treatment of the human body by therapy and thus relate to a subject matter which this International Searching Authority is not required, under the provisions of Article 17(2)(a)(i) of the PCT (continued to extra sheet)

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III **Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

Continuation of Box No.II-1 of continuation of first sheet(2)

and Rule 39.1(iv) of the Regulations under the PCT, to search.

<<Scope of search>>

Claims 1, 12, 13 and 23 relate to a medicine for enhancing the cytotoxic activity of antibody drug in the antibody therapy for cancer, wherein a "lactoferrin hydrolyzate that can be obtained by hydrolysis of lactoferrin with the use of a hydrolase" and "that in the antibody therapy for cancer, has the efficacy of enhancing the cytotoxic activity of antibody drug" is contained as an active ingredient. In this connection, as the composition of hydrolyzate obtained by hydrolysis of lactoferrin can be various depending on the type of hydrolase, hydrolysis conditions, etc., it appears that a large variety of compositions are comprehended in the above "lactoferrin hydrolyzate". However, only the hydrolyzate obtained by hydrolysis under specified conditions with the use of pepsin being a particular hydrolase is fully supported by the description within the meaning of PCT Article 6 and fully disclosed therein within the meaning of PCT Article 5.

On the other hand, claims 8, 12, 20 and 24 relate to a medicine for enhancing the cytotoxic activity of antibody drug in the antibody therapy for cancer, wherein one type or two or more types of peptides satisfying any of the requirements (a) to (d) are contained as an active ingredient. In this connection, it appears that the peptides satisfying any of the requirements (a) to (d) cover various peptides having differentiated lengths and sequence patterns. However, only employment of mixtures containing extremely limited peptides obtained by hydrolysis of lactoferrin under specified conditions, namely, peptides of SEQ ID NOS. 2 and 3 is fully supported by the description within the meaning of PCT Article 6 and fully disclosed therein within the meaning of PCT Article 5.

Therefore, search on claims 1-24 has been substantially restricted to the interaction between lactoferrin hydrolyzate and antibody and/or complement and to medicines for enhancing the cytotoxic activity of antibody drug in the antibody therapy for cancer, wherein a peptide of 25 or 26 sequential amino acid length composed of an amino acid sequence of SEQ ID NO. 2 or 3 is contained as an active ingredient.